REMARKS

By the present communication, claims 1, 6, 7, 13, 20-24, 39, 40 and 50-56 have been amended, claims 10, 14, 35-38, 41 and 42 have been cancelled, and new claims 57-77 have been added in order to define Applicants' invention with greater particularity. No new matter is presented by the proposed amendments submitted herewith as all amended claim language is fully supported by Applicants' specification and original claims. A copy of the claims with markings to indicate the changes made to the claims is attached hereto in Appendix A.

Upon entry of the amendment, claims 1-9, 11-13, 15-24, 39, 40 and 47-77 will be pending, and these claims are presented for the Examiner's convenience as Exhibit B.

Accordingly, in view of the above amendments and remarks, prompt consideration and favorable action on all claims is respectfully requested. In the event any issues remain to be resolved, the Examiner is invited to contact the undersigned at the number provided below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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Enclosures

APPENDIX B: CLAIMS AS THEY WILL STAND UPON ENTRY OF AMENDMENT

1. A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR); and

(ii) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element;

said method comprising providing to the cell an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in the cell; and wherein said one or more ligands are not toxic to said cell.

2. A method according to claim 1 wherein said modified ecdysone receptor comprises:

(i) a ligand binding domain capable of binding an ecdysteroid;

(ii) a DNA-binding domain obtained from a DNA-binding protein; and

(iii) an activation domain of a transcription factor,

wherein at least one of said DNA-binding domain or said activation domain is not obtained from a native ecdysone receptor,

with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein.

3. A method according to claim 2 wherein said modified ecdysone receptor is further characterized as having substantially no constitutive activity in mammalian cells.

4. A method according to claim 2 wherein the DNA-binding domain of said modified ecdysone receptor is derived from a member of the steroid/thyroid hormone superfamily of receptors.

5. A method according to claim 2 wherein said activation domain is obtained from a member of the steroid/thyroid hormone superfamily of receptors.

6. A method according to claim 2 wherein said activation domain is a glucocorticoid receptor activation domain, a VP16 activation domain or a GAL4 activation domain.

7. A method according to claim 6 wherein said modified ecdysone receptor is VpEcR, VgEcR or GecR.

8. A method according to claim 7 wherein said modified ecdysone receptor is VgEcR having the amino acid sequence set forth in SEQ ID NO:5.

9. A method according to claim 1 wherein said modified ecdysone receptor is present primarily in the form of a homodimer.

11. A method according to claim 47, wherein said receptor capable of acting as a silent partner is RXR.

12. A method according to claim 11 wherein said RXR is exogenous to said cell.

13. A method according to claim 1 wherein said response element is a modified response element which comprises, in any order, a first half-site and a second half-site separated by a spacer of 0-5 nucleotides;

wherein said first half-site has the sequence:

-RGBNNM-,

wherein

each R is independently selected from A or G;

each B is independently selected from G, C, or T;

each N is independently selected from A, T, C, or G; and

each M is independently selected from A or C;

with the proviso that

at least 4 nucleotides of each -RGBNNM- group of nucleotides are identical with the nucleotides at comparable positions of the sequence -AGGTCA-; and

said second half-site is obtained from a glucocorticoid receptor subfamily response element.

15. A method according to claim 1 wherein said ligand is a naturally occurring ecdysone, an ecdysone-analog or an ecdysone mimic.

16. A method according to claim 15 wherein said naturally occurring ecdysone is α-ecdysone or β-ecdysone.

17. A method according to claim 15 wherein said ecdysone analog is ponasterone A, ponasterone B, ponasterone C, 26-iodoponasterone A, muristerone A, inokosterone or 26-mesylinokosterone.

18. A method according to claim 15 wherein said ecdysone mimic is 3,5-di-tert-butyl-4-hydroxy-N-isobutyl-benzamide, 8-O-acetylharpagide, a 1,2-diacyl hydrazine, an N′-substituted-N,N′-disubstituted hydrazine, a dibenzoylalkyl cyanohydrazine, an N-substituted-N-alkyl-N,N-diaroyl hydrazine, an N-substituted-N-acyl-N-alkyl, carbonyl hydrazine or an N-aroyl-N′-alkyl-N′-aroyl hydrazine.

19. A method according to claim 1 wherein said exogenous gene is a wild type gene and/or therapeutic gene.

20. A method according to claim 19 wherein said wild type gene encodes products:

the substantial absence of which leads to the occurrence of a non-normal state in said cell; or

a substantial excess of which leads to the occurrence of a non-normal state in said cell.

21. A method according to claim 19 wherein said therapeutic gene encodes products:

which are toxic to the cells in which they are expressed; or

which impart a beneficial property to cells in which they are expressed.

22. A method of inducing the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising an exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR);

(ii) DNA encoding a modified ecdysone receptor under the control of an inducible promoter, wherein said modified ecdysone receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element; and

(iii) one or more ligands for said modified ecdysone receptor;

said method comprising subjecting said cell to conditions suitable to induce expression of said modified ecdysone receptor.

23. A method of inducing expression of an exogenous gene in an isolated cell containing a DNA construct containing said exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR), said method comprising introducing into said cell:

a modified ecdysone receptor; and

one or more ligands for said modified ecdysone receptor,

wherein said receptor, in combination with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element, activating transcription therefrom.

24. A method for the expression of a recombinant product detrimental to isolated host cells, said method comprising:

transforming suitable isolated host cells with:

(i) a DNA construct encoding said recombinant product under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR), and

(ii) DNA encoding a modified ecdysone receptor;

growing said host cells in suitable media; and

inducing expression of said recombinant product by introducing into said host cells one or more ligands for said modified ecdysone receptor, and optionally a receptor capable of acting as a silent partner for said modified ecdysone receptor.

39. A method according to claim 13, wherein said first half-site is obtained from an ecdysone response element and said second half-site is obtained from a glucocorticoid response element, a mineralocorticoid response element, a progesterone response element or an androgen response element.

40. A method according to claim 39, wherein said second half-site is obtained from a glucocorticoid response element.

47. A method according to claim 1, wherein said receptor capable of acting as a silent partner is present.

48. A method according to claim 47 wherein said receptor capable of acting as a silent partner is ultraspiracle.

49. A method according to claim 1 wherein said modified ecdysone receptor has substantially no binding affinity for endogenous response elements.

50. A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element; and

(ii) a modified receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor has substantially no binding affinity for endogenous response elements;

said method comprising providing to the cell an effective amount of one or more ligands for said modified receptor; wherein said one or more ligands are not normally present in the cell; and wherein said one or more ligands are not toxic to said cell.

51. A method according to claim 54, wherein said receptor capable of acting as a silent partner is RXR.

52. A method according to claim 54, wherein said receptor capable of acting as a silent partner is ultraspiracle.

53. A method according to claim 50, wherein said cell is a mammalian cell.

54. A method according to claim 50, wherein said receptor capable of acting as a silent partner is present.

55. A method according to claim 51, wherein said RXR is exogenous to said cell.

56. A method according to claim 50 wherein said modified receptor comprises:

(i) a ligand binding domain capable of binding an ecdysteroid;

(ii) a DNA-binding domain derived from a DNA-binding protein, wherein said DNA-binding domain has substantially no binding affinity for endogenous response elements; and

(iii) an activation domain of a transcription factor,

with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein.

57. A method according to claim 56 wherein said modified receptor is further characterized as having substantially no activity in mammalian cells.

58. A method according to claim 56 wherein the DNA-binding domain of said modified receptor is derived from a member of the steroid/thyroid hormone superfamily of receptors.

59. A method according to claim 56 wherein said activation domain is derived from a member of the steroid/thyroid hormone superfamily of receptors.

60. A method according to claim 56 wherein said activation domain is a glucocorticoid receptor activation domain, a VP16 activation domain or a GAL4 activation domain.

61. A method according to claim 50, wherein said ecdysone response element has substantially no binding affinity for farnesoid X receptor (FXR).

62. A method according to claim 50 wherein said modified receptor has an altered DNA binding specificity relative to the wildtype receptor from which it is derived.

63. A method according to claim 50 wherein said modified receptor is present primarily in the form of a homodimer.

64. A method according to claim 50 wherein said exogenous gene is a wild type gene and/or therapeutic gene.

65. A method according to claim 64 wherein said wild type gene encodes products:

the substantial absence of which leads to the occurrence of a non-normal state in said cell; or

a substantial excess of which leads to the occurrence of a non-normal state in said cell.

66. A method according to claim 64 wherein said therapeutic gene encodes products:

which are toxic to the cells in which they are expressed; or

which impart a beneficial property to cells in which they are expressed.

67. A method of inducing the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising an exogenous gene under the control of an ecdysone response element,

(ii) DNA encoding a modified receptor under the control of an inducible promoter, wherein said modified receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor has substantially no binding affinity for endogenous response elements;

(iii) one or more ligands for said modified receptor;

said method comprising subjecting said cell to conditions suitable to induce expression of said modified receptor.

68. A method of inducing expression of an exogenous gene in an isolated cell containing a DNA construct containing said exogenous gene under the control of an ecdysone response element, said method comprising introducing into said cell:

a modified receptor, wherein said modified receptor has substantially no binding affinity for endogenous response elements; and

one or more ligands for said modified receptor,

wherein said modified receptor, in combination with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, activating transcription therefrom.

69. A method for the expression of a recombinant product detrimental to isolated host cells, said method comprising:

transforming suitable isolated host cells with:

(i) a DNA construct encoding said recombinant product under the control of an ecdysone response element, and

(ii) DNA encoding a modified receptor, wherein said modified receptor has substantially no binding affinity for endogenous response elements; and

growing said host cells in suitable media; and

inducing expression of said recombinant product by introducing into said host cells one or more ligands for said modified ecdysone receptor, and optionally a receptor capable of acting as a silent partner for said modified ecdysone receptor.

70. A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element; and

(ii) a modified receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element wherein said modified receptor has substantially no constitutive activity in mammalian cells,

said method comprising providing to the cell an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in the cell; and wherein said one or more ligands are not toxic to said cell.

71. A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element; and

(ii) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor has an altered DNA binding specificity relative to the wildtype receptor from which it is derived;

said method comprising providing to the cell an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in the cell; and wherein said one or more ligands are not toxic to said cell.

72. A method for modulating the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising said exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR); and

(ii) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element;

said method comprising providing to said subject an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in said subject; and wherein said one or more ligands are not toxic to said subject.

73. A method of inducing the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising an exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR);

(ii) DNA encoding a modified ecdysone receptor under the control of an inducible promoter, wherein said modified ecdysone receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element; and

(iii) one or more ligands for said modified ecdysone receptor;

said method comprising subjecting said subject to conditions suitable to induce expression of said modified ecdysone receptor.

74. A method of inducing expression of an exogenous gene in a mammalian subject containing a DNA construct containing said exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR), said method comprising introducing into said subject:

a modified ecdysone receptor; and

one or more ligands for said modified ecdysone receptor,

wherein said modified ecdysone receptor, in combination with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element, activating transcription therefrom.

75. A method for modulating the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecydsone response element; and

(ii) a modified receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element, wherein said modified receptor has substantially no binding affinity for endogenous response elements;

said method comprising providing to said subject an effective amount of one or more ligands for said modified receptor; wherein said one or more ligands are not normally present in said subject; and wherein said one or more ligands are not toxic to said subject.

76. A method of inducing the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising an exogenous gene under the control of an ecdysone response element,

(ii) DNA encoding a modified receptor under the control of an inducible promoter, wherein said modified receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor has substantially no binding affinity for endogenous response elements;

(iii) one or more ligands for said modified receptor;

said method comprising subjecting said subject to conditions suitable to induce expression of said modified receptor.

77. A method of inducing expression of an exogenous gene in a mammalian subject containing a DNA construct containing said exogenous gene under the control of an ecdysone response element, said method comprising introducing into said subject:

a modified receptor, wherein said modified receptor has substantially no binding affinity for endogenous response elements; and

one or more ligands for said modified receptor,

wherein said modified receptor, in connection with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, activating transcription therefrom.

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APPENDIX A: VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of a **[n ecdysone]** response element, **wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR)**; and

(ii) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said **[ecdysone]** response element;

said method comprising providing to the cell an effective amount of **[a ligand]** **one or more ligands** for said modified ecdysone receptor; wherein said **[ligand is]** **one or more ligands are** not normally present in the cell; and wherein said **[ligand is]** **one or more ligands are** not toxic to said cell.

6. (Amended) A method according to claim 2 wherein said activation domain is **[selected from]** a glucocorticoid receptor activation domain, a VP16 activation domain or a GAL4 activation domain.

7. (Amended) A method according to claim 6 wherein said modified ecdysone receptor is **[selected from]** VpEcR, VgEcR or GecR.

10. **(Cancelled)**

13. (Amended) A method according to claim 1 wherein said **[ecdysone]** response element is a modified response element which comprises, in any order, a first half-site and a second half-site separated by a spacer of 0-5 nucleotides;

wherein said first half-site has the sequence:

-RGBNNM-,

wherein

each R is independently selected from A or G;

each B is independently selected from G, C, or T;

each N is independently selected from A, T, C, or G; and

each M is independently selected from A or C;

with the proviso that

at least 4 nucleotides of each -RGBNNM- group of nucleotides are identical with the nucleotides at comparable positions of the sequence -AGGTCA-; and

said second half-site is obtained from a glucocorticoid receptor subfamily response element.

14. **(Cancelled)**

20. (Amended) A method according to claim 19 wherein said wild type gene **[is selected from genes which]** encodes products:

the substantial absence of which leads to the occurrence of a non-normal state in said cell; or

a substantial excess of which leads to the occurrence of a non-normal state in said cell.

21. (Amended) A method according to claim 19 wherein said therapeutic gene **[is selected from genes which]** encodes products:

which are toxic to the cells in which they are expressed; or

which impart a beneficial property to **[said]** cells **in which they are expressed**.

22. (Amended) A method of inducing the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising an exogenous gene under the control of a[**n ecdysone**] response element, **wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR)**;

(ii) DNA encoding a modified ecdysone receptor under the control of an inducible promoter, wherein said modified ecdysone receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said [**ecdysone**] response element; and

(iii) [**a ligand**] **one or more ligands** for said modified ecdysone receptor;

said method comprising subjecting said cell to conditions suitable to induce expression of said modified ecdysone receptor.

23. (Amended) A method of inducing expression of an exogenous gene in an isolated cell containing a DNA construct containing said exogenous gene under the control of a[**n ecdysone**] response element, **wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR)**, said method comprising introducing into said cell:

a modified ecdysone receptor; and

[**a ligand**] **one or more ligands** for said modified ecdysone receptor,

wherein said receptor, in combination with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said [**ecdysone**] response element, activating transcription therefrom.

24. (Amended) A method for the expression of a recombinant product detrimental to isolated host cells, said method comprising:

transforming suitable isolated host cells with:

(i) a DNA construct encoding said recombinant product under the control of a **[n ecdysone]** response element, **wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR)**, and

(ii) DNA encoding a modified ecdysone receptor;

growing said host cells in suitable media; and

inducing expression of said recombinant product by introducing into said host cells **[ligand(s)] one or more ligands** for said modified ecdysone receptor, and optionally a receptor capable of acting as a silent partner for said modified ecdysone receptor.

35. **(Cancelled)**

36. **(Cancelled)**

37. **(Cancelled)**

38. **(Cancelled)**

39. (Amended) A method according to claim 13, wherein said first half-site is obtained from an ecdysone response element and said second half-site is obtained from a **[hormone response element selected from a]** glucocorticoid response element, a mineralocorticoid response element, a progesterone response element or an androgen response element.

40. A method according to claim 39, wherein said **[first half-site is obtained from an ecdysone response element and said]** second half-site is obtained from a glucocorticoid response element.

41. **(Cancelled)**

42. **(Cancelled)**

50. (Amended) A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element; and

(ii) a modified **[ecdysone]** receptor which, in the presence of a ligand therefor, and **optionally** in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, **wherein said modified receptor has substantially no binding affinity for endogenous response elements**;

said method comprising providing to the cell an effective amount of **[a ligand]** **one or more ligands** for said modified **[ecdysone]** receptor; wherein said **[ligand is]** **one or more ligands are** not normally present in the cell; and wherein said **[ligand is]** **one or more ligands are** not toxic to said cell.

51. A method according to claim **[50]** **54**, wherein said receptor capable of acting as a silent partner is RXR.

52. (Amended) A method according to claim **[52]** **54**, wherein said receptor capable of acting as a silent partner is ultraspiracle.

53. (Amended) A method **according to claim 50, wherein said cell is a** **[for modulating the expression of an exogenous gene in an isolated]** **mammalian cell containing:**

(i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element, and

(ii) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element,

said method comprising providing to said mammalian cell an effective amount of a ligand for said modified ecdysone receptor; wherein said ligand is not normally present in said mammalian cell; and wherein said ligand is not toxic to said] mammalian cell.

54. (Amended) A method according to claim **[1]** 50, wherein said receptor capable of acting as a silent partner is present.

55. (Amended) A method according to claim **[54]** 51, wherein said **[receptor capable of acting as a silent partner is]** RXR is exogenous to said cell.

56. (Amended) A method according to claim 50 **[54,]** wherein said modified receptor comprises:

(i) a ligand binding domain capable of binding an ecdysteroid;

(ii) a DNA-binding domain derived from a DNA-binding protein, wherein said DNA-binding domain has substantially no binding affinity for endogenous response elements; and

(iii) an activation domain of a transcription factor,

with the proviso that when said activation domain is derived from a glucocorticoid receptor, said DNA-binding domain is not derived from a glucocorticoid receptor or an E. coli LexA protein **[is ultraspiracle]**.

Claims 57-77 have been added by the present amendment:

57. (New) A method according to claim 56 wherein said modified receptor is further characterized as having substantially no activity in mammalian cells.

58. (New) A method according to claim 56 wherein the DNA-binding domain of said modified receptor is derived from a member of the steroid/thyroid hormone superfamily of receptors.

59. (New) A method according to claim 56 wherein said activation domain is derived from a member of the steroid/thyroid hormone superfamily of receptors.

60. (New) A method according to claim 56 wherein said activation domain is a glucocorticoid receptor activation domain, a VP16 activation domain or a GAL4 activation domain.

61. (New) A method according to claim 50, wherein said ecdysone response element has substantially no binding affinity for farnesoid X receptor (FXR).

62. (New) A method according to claim 50 wherein said modified receptor has an altered DNA binding specificity relative to the wildtype receptor from which it is derived.

63. (New) A method according to claim 50 wherein said modified receptor is present primarily in the form of a homodimer.

64. (New) A method according to claim 50 wherein said exogenous gene is a wild type gene and/or therapeutic gene.

65. (New) A method according to claim 64 wherein said wild type gene encodes products:

the substantial absence of which leads to the occurrence of a non-normal state in said cell; or

a substantial excess of which leads to the occurrence of a non-normal state in said cell.

66. (New) A method according to claim 64 wherein said therapeutic gene encodes products:

which are toxic to the cells in which they are expressed; or

which impart a beneficial property to cells in which they are expressed.

67. (New) A method of inducing the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising an exogenous gene under the control of an ecdysone response element,

(ii) DNA encoding a modified receptor under the control of an inducible promoter, wherein said modified receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor has substantially no binding affinity for endogenous response elements;

(iii) one or more ligands for said modified receptor;

said method comprising subjecting said cell to conditions suitable to induce expression of said modified receptor.

68. (New) A method of inducing expression of an exogenous gene in an isolated cell containing a DNA construct containing said exogenous gene under the control of an ecdysone response element, said method comprising introducing into said cell:

a modified receptor, wherein said modified receptor has substantially no binding affinity for endogenous response elements; and

one or more ligands for said modified receptor,

wherein said modified receptor, in combination with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, activating transcription therefrom.

69. (New) A method for the expression of a recombinant product detrimental to isolated host cells, said method comprising:

transforming suitable isolated host cells with:

(i) a DNA construct encoding said recombinant product under the control of an ecdysone response element, and

(ii) DNA encoding a modified receptor, wherein said modified receptor has substantially no binding affinity for endogenous response elements; and

growing said host cells in suitable media; and

inducing expression of said recombinant product by introducing into said host cells one or more ligands for said modified ecdysone receptor, and optionally a receptor capable of acting as a silent partner for said modified ecdysone receptor.

70. (New) A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element; and

(ii) a modified receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element wherein said modified receptor has substantially no constitutive activity in mammalian cells,

said method comprising providing to the cell an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in the cell; and wherein said one or more ligands are not toxic to said cell.

71. (New) A method for modulating the expression of an exogenous gene in an isolated cell containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecdysone response element; and

(ii) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor has an altered DNA binding specificity relative to the wildtype receptor from which it is derived;

said method comprising providing to the cell an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in the cell; and wherein said one or more ligands are not toxic to said cell.

72. (New) A method for modulating the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising said exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR); and

(ii) a modified ecdysone receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element;

said method comprising providing to said subject an effective amount of one or more ligands for said modified ecdysone receptor; wherein said one or more ligands are not normally present in said subject; and wherein said one or more ligands are not toxic to said subject.

73. (New) A method of inducing the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising an exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR);

(ii) DNA encoding a modified ecdysone receptor under the control of an inducible promoter, wherein said modificd ecdysone receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element; and

(iii) one or more ligands for said modified ecdysone receptor;

said method comprising subjecting said subject to conditions suitable to induce expression of said modified ecdysone receptor.

74. (New) A method of inducing expression of an exogenous gene in a mammalian subject containing a DNA construct containing said exogenous gene under the control of a response element, wherein said response element has substantially no binding affinity for farnesoid X receptor (FXR), said method comprising introducing into said subject:

a modified ecdysone receptor, and

one or more ligands for said modified ecdysone receptor,

wherein said modified ecdysone receptor, in combination with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element, activating transcription therefrom.

75. (New) A method for modulating the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising said exogenous gene under the control of an ecydsone response element; and

(ii) a modified receptor which, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said response element, wherein said modified receptor has substantially no binding affinity for endogenous response

elements;

said method comprising providing to said subject an effective amount of one or more ligands for said modified receptor; wherein said one or more ligands are not normally present in said subject; and wherein said one or more ligands are not toxic to said subject.

76. (New) A method of inducing the expression of an exogenous gene in a mammalian subject containing:

(i) a DNA construct comprising an exogenous gene under the control of an ecdysone response element,

(ii) DNA encoding a modified receptor under the control of an inducible promoter, wherein said modified receptor, in the presence of a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, wherein said modified receptor has substantially no binding affinity for endogenous response elements;

(iii) one or more ligands for said modified receptor;

said method comprising subjecting said subject to conditions suitable to induce expression of said modified receptor.

77. (New) A method of inducing expression of an exogenous gene in a mammalian subject containing a DNA construct containing said exogenous gene under the control of an ecdysone response element, said method comprising introducing into said subject:

a modified receptor, wherein said modified receptor has substantially no binding affinity for endogenous response elements; and

one or more ligands for said modified receptor,

wherein said modified receptor, in connection with a ligand therefor, and optionally in the further presence of a receptor capable of acting as a silent partner therefor, binds to said ecdysone response element, activating transcription therefrom.